IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

First Named Inventor: Dennis S. Fernandez | Examiner: DeJong, Eric S.

Application No.: 10/646,682 | Art Unit: 1631

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Title: **INTEGRATED BIOSENSOR AND SIMULATION SYSTEM FOR DIAGNOSIS AND THERAPY**

Commissioner for Patents
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APPEAL BRIEF

In response to a final rejection mailed on 02/03/2010, Appellant files this appeal brief under 35 U.S.C. § 134(a) and 37 CFR § 41.37 with the appropriate fees under 37 CFR 41.20(b)(2). The Office action mailed 02/03/2010 set out the rejections from which this appeal is taken. Appellant filed a notice of appeal on 05/03/2010.

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I. REAL PARTY IN INTEREST

The real party in interest is Mr. Dennis S. Fernandez, a registered U.S. patent attorney who co-invented and solely owns the present patent application. Mr. Fernandez resides at 1175 Osborn Avenue, Atherton, California 94027.

II. RELATED APPEALS AND INTERFERENCES

None.

III. STATUS OF CLAIMS

In this proceeding, claims 1-35 have been canceled, claims 36-49 are pending, claim 50 has been withdrawn, and claims 51-55 are pending. All pending claims (36-49 and 51-55) stand rejected and are being appealed.

IV. STATUS OF AMENDMENTS

All claims on appeal (Claims 36-49 and 51-55) are provided in the Claims Appendix, as last modified via the 10/05/2009 Amendment and Request for Reconsideration After Non-Final Rejection.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claims argued separately in this appeal are independent claims 36 and 40 (including their respective dependent claims).

The invention resides in an integrated and reconfigurable biosensor and simulation apparatus, and method thereof, that uses automated systems-biology tools to adaptively provide therapeutic or diagnostic outputs. In particular, one aspect of the invention enables the detection of genomic mutations associated with adverse metabolic reactions to cancer therapeutics.

Regarding independent claim 36, the specification teaches an "integrated biosensor-simulation system" (Figure 1a; page 2: lines 20-26; Figures 1b and 2; page 4, lines 1-22; page 6: lines 21-23; page 7: lines 1-21) that "combines one or more sensor[s] to detect various conditions in [the] biological target or host" (Figure 2; page 6: lines 1-19) and uses a "systems-biology platform" (Figure 3a; page 7: lines 3-11; pages 36-38) to "simulate or analyze stored … data using computational biology such as bioinformatics … or other analysis software or hardware tools" (page 7: lines 3-11; page 38: lines 12-17; page 63: lines 12-22) in order to "adaptively" (page 2: line 22; page 12: lines 7-8; page 13: lines 11-21) provide "therapy, diagnosis, or other automated feedback" (Figure 6; page 2: lines 20-23; page 72: lines 3-22; page 73: lines 1-20). The simulator "compares" a

"sensed signal set … against a model" (Figure 3c; page 4: lines 19-22; page 64: lines 14-22) and "applies systems-biology software to verify, model, or analyze, for example, relative [DNA] sequences" (Figure 5; page 4: lines 19-22) to "determine treatment" (Figure 6; page 5: lines 1-2).

In particular, the specification delineates several biosensors that may be incorporated into the implantable biosensor (Figure 5) to analyze DNA, such as the "Northwestern University DNA-Driven Assembly of Biomaterials System" (page 29: lines 6) and the "TMPT genetic test (commercially available from DNA Sciences (Raleigh, NC)" to identify patients at risk for thioguanine toxicity (page 45: lines 18-22; page 46: lines 1-2). The specification also describes how automated bioinformatic software tools, such as GenBank, and BLAST (page 48: lines 2-5 and page 50: lines 1-9) can be used to determine the function of a gene, and how such genomic data can annotated or classified, such as by experimental design or by hypothesis tested (page 48: lines 9-15), in order to diagnose or treat various diseases. Importantly, the specification also describes how such computationally obtained data can be formatted and accessed (page 64: lines 9-13 and 50: lines 4-7), as well as how it can be stored (page 48: lines 17-21) and statistically analyzed using scatter plot matrices or gene ontology charts (page 63: lines 15-20).

Regarding independent claim 40, the specification teaches sensing with an "implantable biosensor" (Figure 1a; page 4: lines 1-9; page 27: lines 3-4 and 19-22) a "biological target" (Figure 2: pages 14-26, inclusive) and "simulating" (page 41: lines 10-11) with a "simulator comprising a systems-biology platform" (Figure 3a; page 7: lines 3-11; pages 36-38) that "reconfigures" (page 12: lines 21-22; page 13: lines 1-2) a "biocatalytic chip" (Figure 4b; page 8-13), a "logic device" (Figures 4a and 4b; page 65: lines 12-22; page 66: lines 16-20), a "tissue scaffold" (Figure 4b: lines 14-22), a "therapeutic reservoir" (Figures 4b and 4c; page 68: lines 13-22; page 69: lines 1-2), a "probe arranger" (page 69: lines 17-22), or a "DNA microarray" (Figure 5: page 71: lines 1-22; page 72: lines 1-2) "using the signal and a model of the target" (page 46: lines 13-23; page 47: lines 1-16; page 51: lines 1-11) to "generate a therapeutic or diagnostic output" (Figures 4c, 4d, 5 and 6; page 43: lines 8-10; page 47: lines 12-16).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Whether claims 36-49 and 51-55 are rejected under the first paragraph of 35 U.S.C. § 112, as failing to comply with the written description requirement.

2. Whether claims 36-49 and 51-55 are rejected under the second paragraph of 35 U.S.C. § 112, as failing to comply with the written description requirement.

3. Whether claims 36-49 and 51-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Porat (U.S. Patent No. 6,432,050) in view of Giuffre *et al.* (U.S. Patent No. 6,042,548).

VII. ARGUMENT

Statement of Facts

The patent application 10/646,682 that is the subject of this present appeal was originally filed on 08/22/2003. Formal drawings were submitted on 11/04/2003. A Preliminary Amendment was filed on 08/10/2004, which added Claims 11-20. The 02/28/2006 Requirement for Restriction/Election required a choice between Claims 1-10 and Claims 11-20. On 03/14/2006, Appellant elected Claims 1-10 without traverse and withdrew Claims 11-20 from further consideration.

On 05/18/2006, the Examiner rejected Claims 1-10 under the first and second paragraphs of 35 U.S.C. § 112 because the "claims were too broad" and the specification did not provide specific guidance as to what biosensor and assays would be used. The Examiner also rejected Claims 1-2, 4-7, and 9-10 under 35 U.S.C. 102(b) as being anticipated in light of Giuffre (U.S. Patent No. 6,042,548). Appellant responded on 09/01/2006 by filing an Amendment/Request for Reconsideration After Non-Final Rejection which cancelled Claims 1-10 and added new claims 21-35. This was deemed non-responsive under MPEP § 821.03 and the Examiner subsequently granted one month to file a complete response. On 05/29/2007, Appellant filed a revised Amendment/Request for Reconsideration After Non-Final Rejection which

cancelled Claims 1-35 and added Claims 36-43 directed to an integrated and reconfigurable sensor and simulation system and method. The Examiner responded to these changes by issuing a Non-Final Rejection on 08/08/2007 and rejecting Claims 40-43 under 35 U.S.C. § 101 and 35 U.S.C. § 112, second paragraph. Additionally, the Examiner rejected Claims 36-43 as anticipated under 35 U.S.C. 102(b) in light of Giuffre (U.S. Patent No. 6,042,548).

On 09/04/2007, a telephonic interview took place between Examiner Eric S. DeJong and Appellant's representative Ray Akhavan, during which potential amendments to the claims were discussed but no agreement was reached. On 10/29/2007, Appellant filed an Amendment/Request for Reconsideration After a Non-Final Rejection which added new Claims 44-55 to overcome objections under 35 U.S.C. §§ 101 and 102(b). In particular, Appellant argued that Giuffre (U.S. Patent No. 6,042,548) did not anticipate the pending claims where the simulator in Giuffre did not reconfigure any sensor but instead merely constructed a hybrid signal from two different sensors.

On 01/29/2008, a Requirement for Restriction/Election was mailed which required Appellant to choose one location for implantation of the claimed sensor, one kind of biological target, and one species of reconfiguration. Appellant's 02/15/2008 Response to Restriction Requirement elected blood vessel as the implantation site, metabolite as the biological target, and

activation/deactivation as the species of sensor reconfiguration. All elections were made without traverse. On 05/14/2008, the Examiner issued a Final Rejection which withdrew the first and the second species election requirements made on 01/29/2008 and noted that Claim 50 was withdrawn because it was drawn to a non-elected species. The rejections based on 35 U.S.C. § 112 and 35 U.S.C. § 101 were withdrawn, but all pending claims were nonetheless rejected under 35 U.S.C. § 102(b) as anticipated in light of Giuffre, where Giuffre taught the deactivation of brain-associated neurosensors following the training of a neural network. Appellant's 07/10/2008 Response to Final Action traversed the Examiner's rejection based on 35 U.S.C. § 102(b) by arguing that Giuffre teaches away from invasive monitoring while the present invention concerns an implantable biosensor, and by arguing that biosensor reconfiguration means activating or deactivating a sensor more than once. The Examiner responded with an Advisory Action mailed 08/07/2008 which declared that a Request for Continued Examined should be filed in order to place the application in a condition for allowance. The Examiner further reaffirmed the claim rejections under 35 U.S.C. § 102(b) by arguing that the claims were not limited to an implantable device and the specification and claims did not narrowly define reconfiguration so as to require more than one activation or deactivation of a sensor. Appellant filed an Amendment/Request for Continued Examination on

08/25/2008 and amended Claims 36 and 40 to distinguish them from the prior art by requiring that the sensor be "implantable" and clarifying that sensor reconfiguration expressly involved "reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, a therapeutic reservoir, or a DNA microarray."

On 12/02/2008, a Non-Final Rejection was issued withdrawing prior objections based on 35 U.S.C. § 102(b) and rejecting all claims under 35 U.S.C. § 103(a) as obvious where Porat et al. (described an implantable biosensor system capable of operating a shunt, which read on a reconfigurable therapeutic reservoir, and where Giuffre's programmable computer system for simulation of brain activity read on a simulator comprising a systems-biology platform and a model to generate a therapeutic output. Appellant responded on 12/15/2008 by amending independent Claims 36 and 40 to distinguish them from Porat by removing the "therapeutic reservoir" limitation and by specifying more particularly that the simulator was directed to a "systems biology platform" that automatically integrates target biosensing with in-vivo modeling. However, this response failed to include a list of all pending claims (including withdrawn claims) and a Notice of Non-Compliant Amendment was issued on 01/29/2009. On 02/12/2009, Appellant submitted a complaint Amendment.

On 05/27/2009, a Final Rejection was mailed, which simply re-iterated the rejection of pending Claims 36-49 and 51-55 under 35 U.S.C. § 103(a) as

obvious in light of Porat and Giuffre. Although the claims had been amended on 01/29/2009 to remove the "therapeutic reservoir" limitation and distinguish Porat, the Examiner apparently did not realize this and continued to argue that Porat's implantable biosensor and operable shunt read on an implantable biosensor with a simulator capable of reconfiguring a therapeutic reservoir. The Examiner dismissed the "systems-biology platform" limitation by arguing that the programmable computer system for simulation in Giuffre was the functional equivalent of a systems biology platform.

In a 07/23/2009 Request for Continued Examination, Appellant amended independent Claims 36 and 40 to further distinguish Giuffre by specifying that the systems-biology platform was comprised of components related to ten different scientific fields. The amendments also added two additional elements that could be reconfigured by the simulator: a therapeutic reservoir and a probe arranger. In a 09/02/2009 Non-Final Rejection, the Examiner rejected Claims 36-49 and 51-55 under the first paragraph of 35 U.S.C. § 112 by claiming that the amendments related to the ten different scientific fields lacked any support in the specification and constituted new matter. The Examiner also rejected Claims 26-49 and 51-55 under the second paragraph of 35 U.S.C. § 112 by claiming that the amendment to add the ten scientific fields did not place any meaningful limits on the systems-biology platform. Lastly, the Examiner again

rejected all pending claims as obvious in light of Porat and Giuffre because the proposed distinguishing amendments of 07/23/2009 did limit the claims so as to distinguish them from the prior art.

On 10/05/2009, Appellant submitted an Amendment/Request for Reconsideration After Non-Final Rejection which amended independent Claims 36 and 40 to specify that the systems-biology platform "comprises computational modeling hardware and software analysis genomics ... and transcriptomics automated tools ...." In addition to adding these structural and functional limitations to the systems-biology platform, Appellant contended that neither Porat nor Giuffre teach, suggest or motivate a systems-biology platform involving automated hardware and software tools chosen from the ten listed scientific fields. In response, the Examiner issued a Final Rejection on 02/03/2009 which: (1) rejected Claims 36-49 and 51-55 under the first paragraph of 35 U.S.C. § 112 because the claim amendments made on 10/05/2009 and 07/23/2009 lacked any support in the specification and constituted new matter and did not identify "actual, meaningful elements" that limited the scope of the claimed invention; (2) rejected Claims 36-49 and 51-55 under the second paragraph of 35 U.S.C. § 112 because the scope of the claimed computational hardware and software was not defined in the specification and did not identify "actual, meaningful elements" of the claimed

invention; and (3) rejected Claims 36-49 and 51-55 as under 35 U.S.C. § 103(a) as unpatentable over Porat *et al.* in view of Giuffre because the amendments of 10/05/2009 and 07/23/2009 to the systems-biology platform were too broad and thus did not patentably distinguish the instant claims from the prior art.

A. Rejection Under the First Paragraph of 35 U.S.C. § 112 is Improper When the Examiner Fails to Establish a *Prima Facie* Case

1. All claim amendments are amply supported by the specification.

Appellant amended claims 36 and 40 on 07/23/2009 and 10/05/2009 to specify that the systems-biology platform "comprises computational modeling hardware and software analysis … automated tools," including those pertaining to genomics, proteomics, computational chemistry, and seven other related fields. (07/23/2009 Amendment and Request for Continued Examination and 10/05/2009 Amendment and Request for Reconsideration After Non-Final Rejection).

The support for these 07/23/2009 and 10/05/2009 amendments initially stems from the Background section of the specification, which notes that in the prior art, biological sensors have not been "easily or automatically integrated or reconfigurable" with "systems-biology software [that] provides computational modeling for genomics, proteomics, metabolomics, transcriptomics, computational chemistry, [and] pharmacogenomics … for interdisciplinary diagnosis or therapy." (Specification, page 2: lines 13-18 (emphasis added)). In light of this problem in the field, the summary of the invention points out that the essence of Appellant's

invention is an "integrated biosensor-simulation system" that uses systems-biology "software programs" to monitor and model a target and provide adaptive and "automated feedback." (Specification, page 2: lines 20-26).

Significant and detailed support for this automated systems-biology tools limitation on claims 36 and 40 is found throughout the specification. As Figure 3a and pages 36-38 of the specification make clear, the systems-biology platform component of the biosensor can be made up of one or more "software components" "for analyzing [the] genomics 301, proteomics 302, computational chemistry 303, pharmacogenomics 304, computational biology 305, computational biophysics 306, computational cell behavior 307, pharmacokinetics 308, metabolomics 309, transcriptomics 310, bioinformatics 311, [or] other computational behavior of the biological system." (Specification, Figure 3a, and pages 36-38). This systems-biology software is used by the biosensor to "verify, model, or analyze, for example, relative sequences, 3-dimensional structure, [or] molecular interactions …." (Specification, page 4: lines 19-22).

As a first example, bioinformatics is listed in the specification as one of several "computational biology…analysis software… tools" (Specification, page 7: lines 3-6) that "provides information content or flow in biological systems and processes …." (Specification, page 38: lines 12-17). The specification delineates several bioinformatic automated tools, such as GenBank, Unigene, LocusLink,

HomoloGene, Ensemble, GoldenPath, NCICB Cancer Genome Anatomy Project, and BLAST (Specification, page 48: lines 2-5 and page 50: lines 1-9) that can be used in bioinformatic or proteomic embodiments of the claimed invention to determine the hypothetical function of a gene or protein by finding its similarity to other known genes or proteins. (Specification, page 50: lines 11-15). Not only are readers told which bioinformatic programs they can use, they are also given examples of how this systems-biology platform data may be annotated or classified, such as by experimental design or by hypothesis tested. (Specification, page 48: lines 9-15).

As a second example, the specification suggests how to use proteomics-based automated tools to determine the presence, structure, and function of disease-related proteins or peptides. (Specification, page 37: lines 6-10; and page 19: lines 16-22 (explaining how automated SELDI-TOF mass spectrometry can be used to distinguish between protein fragments derived from normal versus cancerous samples of breast fluids, where cancerous fragments have a higher mass than normal fragments), page 20: lines 1-9 (similarly describing how to detect prostate cancer using the exact mass of a prostate cancer-related protein), page 50: lines 17-21 (indicating how protein samples should be cleaved, purified via high pressure liquid chromatography, and separated by gel electrophoresis for quantitative analysis using mass spectrometry-based equipment)). The

specification also allows for the possibility of using other kinds of automated mass spectrometry tools such as electrospray ionization tandem mass spectrometry (ESI-MS) on triple or quadruple or ion trap mass spectrometers (Specification, page 29: lines 17-22).

Importantly, the specification also describes how computationally obtained data can be formatted using standardization programs such as the MicroArray and Gene Expression Markup Language (MAGE-ML) and accessed using a proper annotation format such as DAS ("Distributed Annotation System") (Specification, page 64: lines 9-13 and 50: lines 4-7), as well as how it can be stored and exchanged using the specifications provided by the Interoperable Informatics Infrastructure Consortium (I3C). (Specification, page 48: lines 17-21). The specification also suggests how the data obtained by the systems-biology platform from these automated tools can be statistically analyzed using, for example, scatter plot matrices or gene ontology charts. (Specification, page 63: lines 15-20). Appellant contends that although the initial limitation for the automated systems-biology tools resided in the ten listed scientific fields, the number of automated tools available for each field was limited to a small number at the time this application was filed, and the specification provided sufficient examples to enable the entire genus of integrated systems-biology platform based biosensors.

Furthermore, the specification also details the hardware that makes up both the implantable network biosensor (Specification, Figure 1a) and its integrated systems-biology platform (Specification, Figures 3a, 3c, 4a, 4d, and 5). For example, the biosensor "generally comprises [a] biological microelectromechanical (bioMEMs) sensor chip or detection or transducer device" made of silica, glass, or other polymer. (Specification, page 30: lines 16-22). This includes a biosensor platform with a multifunctional array of sensors coupled to a detection system (Specification, Figures 1a and 2). For example, one of the possible sensors in the biosensor platform can be a DNA sensor "to profile for changes in methylation, monitor gene expression, … scan the whole genome including micro-array-based comparative genomic hybridization to measure and map DNA copy number aberrations, detect disease markers, [or] genotype single nucleotide polymorphisms (SNPs)…." (Specification, page 14: lines 18-24; page 15: lines 1-3). For single-nucleotide polymorphism detection, the DNA sensor may apply an "invader platform" or similar device for genetic sequencing (Specification, page 15: lines 22-23). In particular, when discussing the kinds of physical DNA sensors that can be employed, the specification discusses that a system similar to the "Northwestern University DNA-Driven Assembly of Biomaterials System" may be used to attach gold particles to DNA nucleotides in order to create a specific arrangement of probe DNA molecules which are then detectable via an optical device.

(Specification, page 29: lines 1-6). Several kinds of optical devices, such as surface plasmon resonance sensors similar to the BIACORE® system, are mentioned as components for the optical sensor (Specification, page 34: lines 18-23). In addition, the specification also describes RNA, peptide/protein, and antibody sensors, among several others, that may form a part of the biosensor platform, and these sensors also "utilize high-throughput" micro-or-nano arrays, such as the CombiMatrix array or the GeneFluidics 3D micro-fabricated platform with embedded electrochemical sensor array. (Specification, pages 29-30). The systems biology platform "may be integrated within one or more integrated circuit[s], module[s] or processor[s]; or [may] bilaterally communicate to outside non-host signal source through [a] wireless communication unit" (Specification, page 7: lines 8-11). The implantable biosensor may be accessible according to IEEE 1451 network interface format. (Specification, page 5: 20-21). In sum, there is ample graphical and textual support for the amendments made on 07/23/2009 and 10/05/2009; this graphical and textual support, contrary to the Examiner's arguments, provides "particular language that identifies actual, meaningful elements that limit the scope of the claimed invention." (FOA 202/03/2010, page 6).

2. The "computational biology" and "computational biophysics" amendments made 07/23/2009 are not new matter.

The 02/03/2010 Final Office Action also rejected independent claims 36 and 40 under the first paragraph of 35 U.S.C. § 112 because Appellant allegedly did "not provide any support" for either the "computational biology" or "computational biophysics" amendments made to these claims on 07/23/2009. (FOA dated 02/03/2010, pages 3-4). However, this factual finding is clearly erroneous where, as here, these phrases are defined in the text and described in Figure 3a of the specification.

The specification defines both of these phrases by noting that "[c]omputational biology … uses algorithmic tools to facilitate biological analyses," while "[c]omputational biophysics … uses algorithmic tools to facilitate biophysical or biokinetic analyses." (Specification page 37: lines 18-20). Figure 3a in the specification shows that both "computational biology" and "computational biophysics" can comprise parts of the systems biology platform. (Specification, Figure 3a). Additionally, the specification makes clear that the systems biology platform uses "software programs … [to] model, simulate, or analyze stored or raw data using computational biology, such as bioinformatics … or other analysis software … tools." (Specification, page 7: lines 3-6).

Appellant contends that the terms "computational biology" or "computational biophysics" would have been readily understood by a person

having ordinary skill in the art at the time of this application. (*See* NIH Working Definition of Bioinformatics and Computational Biology, July 17, 2000, http://www.bisti.nih.gov/CompuBioDef.pdf on 06/12/2010, accessed on 6/10/2010 (defining computational biology as "the development and application of data-analytical and theoretical methods, mathematical modeling and computational simulation techniques to the study of biological…systems"). In light of the above-cited evidence, Appellant requests that these specific amendments be considered properly supported by the specification and thus not new matter as claimed by the Examiner. (FOA 02/03/2010, page 4).

3. Examiner Rejection Lacking Specific Technical Reasons Why Claims are Not Enabling Cannot Establish *Prima Facie* Case.

The 02/03/2010 Final Office Action rejected the textual and drawing-related support Appellant provided as "merely a reiteration of the terms recited in the instant claims" that did not "amount to any meaningful definition … [and was] limited to broad field of use language and not particular language that identified actual, meaningful elements that limit the scope of the claimed invention." (FOA 02/03/2010, page 4).

Appellant respectfully submits that the specification's support for all claims is apparent and thus the Examiner's decision to disregard this evidence without providing any specific, technical justification fails to satisfy the Examiner's burden of establishing a *prima facie* case. There is a strong presumption that an adequate

written description of the claimed invention is present in the specification as filed. (*Wertheim*, 541 F. 2d 257, 267 (1976); MPEP § 2163 (II)(A)). To rebut this strong presumption, the Examiner must set forth "express findings of fact supporting the alleged lack of written description, and … establish a prima facie case by providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application when filed." (MPEP § 2163 (III)(A) (emphasis added)). The Examiner's response did not provide any evidence in the form of cited publications, affidavits, or specific technical reasons to question the adequacy of Appellant's written description of the invention. (MPEP § 2164.04). In particular, a failure to provide "specific technical reasons" means that no *prima facie* case is established. (MPEP § 2164.04).

B. Rejection of Claims 36-49 and 51-55 Under the Second Paragraph of 35 U.S.C. § 112 is Improper Where the Examiner Applied an Erroneous Enablement Standard

The Examiner similarly rejected claims 36-49 and 51-55 under the second paragraph of 35 U.S.C. § 112 by stating that the 07/23/2009 and 10/05/2009 amendments to independent claims 36 and 40 contained claim limitations that were "undefined and … only limited to broad field of use language" that lacked concrete details about the "components and programming" that make up the invention.

(FOA 02/03/2010, page 5). However, the Examiner again did not provide any factual evidence or technical reasons to support this assertion or his further conclusion that no "meaningful definition" had been imposed on the claimed systems-biology platform. (FOA 02/03/2010, page 6). Simply mentioning the breadth of a claim limitation is not sufficient to establish a violation of the written description requirement. (See *Ex Parte Buechler*, Appeal No. 2003-2084, Application No. 08/241,061 (rejection reversed where examiner merely compared broad scope of claimed "crosstalk inhibitors" with the "narrow scope" of the specific, exemplary crosstalk inhibitors in the specification), accessed on 6/12/2010 at http://www.uspto.gov/go/dcom/bpai/decisions/fd032084.pdf).

Moreover, Appellant respectfully contends that definitions are not required in order to meet the written description requirement of 35 U.S.C. § 112. Both the MPEP and precedential BPAI case law indicate that the mere "absence of definitions … should not be the basis of a rejection under 35 U.S.C. § 112." (MPEP § 2163; see also the precedential decision *Ex Parte Bass*, BPAI Appeal No. 2009-008347, decided 02/16/2010 (reversing Examiner's rejection of a claim under the first paragraph of 35 U.S.C. § 112 where the Examiner simply pointed to the lack of a definition in the specification without providing "persuasive reasoning and/or evidence" to support his conclusion)).

C. Rejection of claims 36-49 and 51-55 under 35 U.S.C. 103(a) as being unpatentable over Porat (U.S. Patent No. 6,432,050) in view of Giuffre et al. (U.S. Patent No. 6,042,548) is Improper

1. Neither Porat Nor Giuffre Teach an Integrated Biosensor Containing a Systems-Biology Platform

The Examiner rejected claims 36-49 and 51-55 as obvious over Porat *et al.* in view of Giuffre because "it would have been obvious to one of ordinary skill…to combine the biosensor and methods" of Porat with the "method and system for registering changes in brain and central nervous system activity using simulation and signals derived from biosensors" as taught by Guiffre. (FOA 02/03/2010, page 10). The Examiner also asserted that the motivation to combine these two prior art sources was provided by Guiffre which teaches that "systems that can predict brain states using already implemented cardiovascular monitoring modalities will allow for predictive capabilities while minimizing risk, cost, and added complexity of such setups." (FOA 02/03/2010).

By the Examiner's own admission, Porat *et al.* "do not expressly teach the use of a simulator comprising a system-biology platform and a model to generate a therapeutic or diagnostic output." (FOA 02/03/2010). However, the Examiner argues that Giuffre's "programmable computer systems for simulation of brain activity using signal data and a model to estimate brain and central nervous system activity" read on "a system-biology platform as recited in Claims 36 and 40." (FOA 02/03/2010).

Appellant argues that the computer-based simulation and modeling of cardiovascular data in Giuffre cannot reasonably be interpreted to cover an integrated biosensor containing a systems-biology platform as described in Appellant's Application No. 10/646,682. Giuffre seeks to create a noninvasive "'virtual' brain monitor" that uses cardiovascular data combined with a model of the patient's brain activity to predict future brain activity under similar cardiovascular conditions. (Giuffre, U.S. Patent No. 6,042,548, Columns 7-8 and Figure 4a). On the other hand, Appellant seeks to create an implantable integrated biosensor with a systems-biology platform (Specification, Figure 1a and page 2: lines 12-26 (emphasis added)). There is no mention in Porat or Giuffre of any of the specific hardware or software tools that pertain to genomics, proteomics, computational chemistry, or the seven related fields listed in Claim 36 and 40. (07/23/2009 Amendment and Request for Continued Examination and 10/05/2009 Amendment and Request for Reconsideration After Non-Final Rejection). Moreover, a person having ordinary skill in the art at the time of this invention would have understood "integrated" to mean "constructed on a single piece of material, such as a semiconductor wafer." (See Illustrated Dictionary of Electronics, 8th ed., (2001) p. 367 (McGraw-Hill)). This is particularly true where, as here, the specification provides clear indication that what was being integrated

was "various sensors" with "systems-biology software" tools for "interdisciplinary diagnosis or therapy." (Specification, page 2: lines 12-26).

2. The Acoustic Biosensor of Porat and the Method and System of Cardiovascular Monitoring of Giuffre Cannot Be Effectively Combined

Appellant further contends that combining the implantable piezoelectric sensor of Porat and the cardiovascular monitoring method of Giuffre will render the piezoelectric sensor unsatisfactory for its intended purpose. (MPEP § 2141 (V)(A)). In such a case, the suggestion or motivation to combine these prior art references does not exist. (See *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984); MPEP § 2143.01). Porat's implantable acoustic sensor has a "substantially flexible piezoelectric layer" of PVDF or piezoceramic (Porat, U.S. Patent No. 6,432,050, Figures 1a, 1b and 6; column 16, lines 52-56). These piezoelectric film layers are susceptible to electromagnetic interference (Images Scientific Instruments Inc., *Piezo Film Sensors Technical Manual*, page 7, downloaded on 06/23/2010 from http://www.imagesco.com/catalog/sensors/piezo.html), such as that caused by Giuffre's preferred method of monitoring cardiac output via "thoracic bioimpedance … [using] … electrodes positioned on the subject and used for electrocardiographic analysis" (Giuffre, U.S. Patent No. 6,042,548, Fig 4b, column 7, lines 4-10 and column 8, lines 3-7). Both at now and at the time of Appellant's invention, the measurement of cardiac output by thoracic impedance

was accomplished by placing electrodes on the patient's chest and neck and injecting a high frequency current (70 kHz, 2.5 mA rms) into the patient's thoracic region (Barry *et al.*, *Lack of Agreement Between Bioimpedance and Continuous Thermodilution Measurement of Cardiac Output in Intensive Care Unit Patients,* Critical Care, 1997 1: 71-74; Stevanovic *et al.*, *Thoracic Electrical Bioimpedance Theory and Clinical Possibilities in Perioperative Medicine*, Signa Vitae, 2008, Volume 3 Supplement 1: 22-27). Such a high frequency current was sufficient to cause a similar implantable piezoelectric cardiac sensor to seriously malfunction (Aldrete *et al.*, *Pacemaker Malfunction Due to Microcurrent Injection from a Bioimpedance Noninvasive Cardic Output monitor*, Journal of Clinical Monitoring, 1995; 11: 131-33). In light of these facts, a person having ordinary skill in the art at the time of this invention would not have considered combining the biosensor of Porat with the cardiovascular monitoring method and system of Giuffre.

3. No Reasonable Expectation of Success Where Prior Art Discouraged Use of Piezoelectric Biosensors for Genomic Applications

Additionally, to reject a claim based on the Examiner's "obvious to try" rationale, the Examiner must articulate: (1) a design need or market pressure to solve a problem, (2) a finding that there had been a finite number of identified, predictable solutions to the problem, and (3) a finding that one of ordinary skill could have pursued the known potential solutions with a reasonable expectation of

success (MPEP § 2143(E)). The Examiner has not produced any evidence that there were a finite number of identified predictable solutions to the problem of how to integrate biosensors with systems-biology software and hardware for interdisciplinary diagnosis or therapy (Specification, Related Background Art and Summary, page 2), nor has he provided any evidence that one of ordinary skill would have had a reasonable expectation of success; such evidence is doubly necessary when, as is the case here, an inventor explores a new technology or approach to innovation with only general guidance from the prior art (*In re O' Farrell*, 853 F.2d 894, 903 (Fed Cir. 1988)).

In fact, the evidence indicates that at the time of this invention, (1) the surfaces of quartz crystal microbalance sensors were ill-suited for use in quantitatively analyzing DNA or RNA because it was difficult to immobilize single-stranded oligonucleotides to them; they typically had surface coverage values of 10% to 30% with detection limits on the order of 10^{-8} moles/liter where the desired detection limit was ten orders of magnitude lower at 10^{-18} moles/liter (Janshoff *et al.*, *Piezoelectric Mass-Sensing Devices as Biosensors – An Alternative to Optical Biosensors?*, Angewandte Chemie International Edition (2000), Volume 39: 4004-4032); (2) QCMs suffered from poor signal to noise ratios (Su *et al.*, *Comparison of Surface Plasmon Resonance Spectroscopy and Quartz Crystal Microbalance Techniques for Studying DNA Assembly and*

Hybridization, Biosensors and Bioelectronics, (2005) Vol. 21: 719-726 (finding that the intrinsic mass sensitivity of a typical QCM was 20 times lower than for a typical instrument utilizing optical spectroscopy); B.R. Eggins, *Chemical Sensors and Biosensors*, (2002), Ch. 7, page 200-203); (3) QCM biosensor surface components were very vulnerable to "local accumulation of surface-active agents from the body such as cells, proteins, and other less well-identified constituents such as colloidal and lipid aggregates…known as 'biofouling"' which would alter and degrade the sensor's response and performance (P. Vadgama, Surfaces and Interfaces for Bio-Materials, (2005) Ch. 5: *Stable use of biosensors at the sample interface*, p. 104-105); and (4) this surface deposition of the body's diffuse cellular biocomponents on the QCM sensor resulted in rapid degradation of sensor function, observed "within minutes and hours rather than days and months" and although the sensor continued to operate, its value as an accurate and precise quantitative system was lost. (Vadgama, p. 106). In view of the significant technological and commercial obstacles to solving the problem addressed by Appellant's invention, the Examiner erred in concluding the claims are obvious in light of Porat and Giuffre. (See *In re Rinehart*, 531 F.2d 1048 (CCPA 1976) (no reasonable expectation of success in combining prior art teachings in view of unchallenged evidence showing that the prior art processes individually could not be successfully

scaled up; see also *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08 (Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991)).

CONCLUSION

For the foregoing reasons, Appellant respectfully requests that the Board reverse the Examiner's rejections under 35 U.S.C. § 112 and 35 U.S.C. § 103(a).

Respectfully Submitted,

Date: ___07/06/2010_____ /Dennis S. Fernandez/

Dennis S. Fernandez
Reg. No. 34,160

VIII. CLAIMS APPENDIX

Listing of Claims:

IX. EVIDENCE APPENDIX

TABLE OF CONTENTS

Office Action Setting-Out Rejection on Appeal

See attached Office action, mailed 02/03/2010.

All Evidence Relied Upon by Examiner in Support of Rejection on Appeal

Examiner has relied upon the following:

Patent/Pub. No.	Issue or Pub. Date	Applicant	Filing Date
US 6432050	08-13-2002	Porat	05-03-1999
US 6042548	03-28-2000	Giuffre	11-14-1997

Relevant Portion of Paper Filed by Appellants Before Examiner Which Shows that Argument Made on Appeal Was Made in First Instance to Examiner

See the attached Amendments/Requests for Reconsideration After Non-Final Rejection, filed on 09/01/2006, 05/29/2007, 10/29/2007, 12/15/2008, 02/12/2009, and 10/05/2009, as well as the Amendments/Requests for Continued Examination, filed on 08/25/2008 and 07/23/2009.

Affidavits and Declarations

None.

Other Evidence Filed Prior to the Notice of Appeal

None.

Other Evidence Filed After the Notice of Appeal

None.

X. RELATED PROCEEDINGS APPENDIX

None.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Fernandez	Attorney Docket No.:	FERN-P013
Serial No:	10/646,682	Group Art Unit:	1631
Filed:	08/22/2003	Examiner:	Miller, Marina I.
Title:	Integrated Biosensor and Simulation System for Diagnosis and Therapy		

AMENDMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action dated May 18, 2006, Applicant petitions for extension of time, pursuant to 37 C.F.R. 1.136, for one month, and respectfully requests this application to be amended as follows:

Amendments to the Specification begin on page 2

Amendments to the Claims begin on page 3.

Remarks begin on page 7.

AMENDMENTS TO THE SPECIFICATION

Please delete paragraph [0168] and replace it with the following amended paragraph:

[0168] Preferably such stored information complies, at least in part, with data exchange and management framework and specifications provided by Interoperable Informatics Infrastructure Consortium (I3C), which technical and use-case model documents, and recommended implementations, as described on-line at ~~http://www.i3c.org/~~ the website of the i3c organization and are hereby incorporated by reference as appropriate herein.

AMENDMENTS TO THE CLAIMS

This listing of claims replaces prior versions, and listings, of claims in the application:

Listing of Claims

1. **(CANCELLED)** Integrated biosensor and simulation system comprising:

   a sensor for sensing a biological target to generate a signal; and

   a simulator for using the signal and a model of the target to generate a therapeutic or diagnostic output.

2. **(CANCELLED)** The system of claim 1 wherein:

   the sensor is reconfigurable by the simulator.

3. **(CANCELLED)** The system of claim 1 wherein:

   the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

4. **(CANCELLED)** The system of claim 1 wherein:

   the simulator generates the output according to a regulatory condition.

5. **(CANCELLED)** The system of claim 1 wherein:

   the sensor couples to the simulator via a programmable switch.

6. **(CANCELLED)** Automated sensor and simulation method comprising the steps of:

sensing a biological target to generate a signal; and

simulating using the signal and a model of the target to generate a therapeutic or diagnostic output.

7. **(CANCELLED)** The method of claim 6 wherein:

a simulator for simulating reconfigures a sensor for sensing.

8. **(CANCELLED)** The method of claim 7 wherein:

the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

9. **(CANCELLED)** The method of claim 7 wherein:

the simulator generates the output according to a regulatory condition.

10. **(CANCELLED)** The method of claim 7 wherein:

the sensor couples to the simulator via a programmable switch.

11. **(WITHDRAWN)** Implantable network-biosensor comprising:

a sensor unit for receiving a multi-sensor signal from a biosensor platform for detecting a biological material of a host; and

a controller for processing a systems-biology platform for verifying or modifying a simulation model associated with the biological material.

12. **(WITHDRAWN)** The network biosensor of claim 11 wherein:

the sensor unit is configurable or programmable for detecting multi-sensor signaling, thereby enabling the biosensor platform to access one or more sensor signals from the group consisting essentially of a DNA or RNA sensor, a peptide or protein sensor, an antibody or antigen sensor, a vector or virus-vector sensor, a lipid or fatty-acid sensor, and an inorganic-ion or electrochemical sensor.

13. **(WITHDRAWN)** The network biosensor of claim 11 wherein:

the sensor unit is configurable or programmable for detecting multi-sensor signaling, thereby enabling the biosensor platform to access one or more sensor signals from the group consisting essentially of a tissue-factor sensor, a steroid sensor, a neurotransmitter sensor, a pH sensor, a free-radical sensor, a carbohydrate sensor, a neural sensor, a chemical sensor, a small-molecule sensor, an exon sensor, a metabolites sensor, an intermediate sensor, a chromosome sensor, and a cell sensor.

14. **(WITHDRAWN)** The network biosensor of claim 11 wherein:

the sensor unit comprises a positioning chip for immobilizing or positioning the biological material for sensing thereof.

15. **(WITHDRAWN)** The network biosensor of claim 11 wherein:

the sensor unit receives another multi-sensor signal from another biosensor platform for detecting another biological material of the same or another host.

16. (**WITHDRAWN**) The network biosensor of claim 11 wherein:

the controller is configurable or programmable for processing multiple simulation applications, thereby enabling the systems-biology platform to access one or more simulation models from the group consisting essentially of a genomics model, a proteomics model, a computational chemistry model, a pharmacogenomics model, a computational biology model, a computational biophysics model, a computational cell behavior model, a pharmacokinetics model, a metabolomics model, and a transcriptomics model.

17. (**WITHDRAWN**) The network biosensor of claim 11 wherein:

the controller is configurable or programmable for processing multiple simulation data, thereby enabling the systems-biology platform to access one or more simulation data from the group consisting essentially of a genetic-disorder or mutation data, an infectious disease or infection data, an immunity-disease data, a single-organ or cell-type autoimmune disease data, and a neoplasia data.

18. (**WITHDRAWN**) The network biosensor of claim 11 further comprising:

a therapeutic unit for releasing or dispensing a therapeutic material from a reservoir in or onto the host, whereby the sensor unit may automatically detect an effect of the therapeutic material on the host.

19. (**WITHDRAWN**) The network biosensor of claim 18 wherein:

the therapeutic unit is configurable or programmable for releasing or dispensing the therapeutic material alternatively from manufacture means, thereby enabling the systems-biology platform to instruct the therapeutic unit configurably or programmably using one or more manufacture-means components from the group consisting essentially of pharmaceuticals, biopharmaceuticals, reconfigurable biocatalytic chips, tissue scaffolds, and micro or nano-array or electro-mechanical tools.

20. (**WITHDRAWN**) The network biosensor of claim 11 wherein:

the controller processes the systems-biology platform adaptively for generating a diagnostic or therapeutic signal or report, whereby the systems-biology platform may access one or more simulation applications from the group consisting essentially of a neural or learning network, a statistical or probabilistic expert, fuzzy-logic or knowledge-based system, an artificial intelligence or decision-making inference-engine or program, and a supervised or unsupervised Bayesian or Markovian analysis, clustering, criterion or classification program.

21. (**NEW**) Sensor apparatus comprising:

a multi-functional array coupled programmably to a peptide or protein sensor, an antibody sensor, a carbohydrate sensor, and a cell sensor.

22. (**NEW**) The apparatus of claim 21 wherein:

the sensor array comprises a reconfigurable hardware switch logically interconnecting a plurality of biosensors to a networked controller.

23. (**NEW**) The apparatus of claim 21 further comprising:

a positioning chip, coupled to one or more of the array sensors.

24. (**NEW**) The apparatus of claim 23 wherein:

the positioning chip comprises a patch clamp.

25. (**NEW**) The apparatus of claim 21 wherein:

the peptide or protein sensor comprises an electrophoresis tag or micro-assay, or protein chip.

26. (**NEW**) The apparatus of claim 21 wherein:

the antibody sensor comprises a phagotope biochip.

27. (**NEW**) The apparatus of claim 21 wherein:

the sensor array couples further to a vector or virus vector sensor comprising a micro-array or assay with known sequenced virus attached, or a micro-array or assay that detects homologs.

28. (**NEW**) The apparatus of claim 21 wherein:

the carbohydrate sensor comprises a glycochip, or a whole blood glucose monitoring system.

29. (**NEW**) The apparatus of claim 21 wherein:

the cell sensor comprises a bionic chip for cell-growth.

30. (**NEW**) The apparatus of claim 21 further comprising:

a therapeutic unit comprising a pill comprising a micro-pump, a polymer scaffold comprising hydrogel, or an implantable bio-MEMs chip comprising a medication reservoir, such unit being coupled to at least one sensor.

31. (**NEW**) The apparatus of claim 21 wherein:

the sensor array couples further to a DNA sensor comprising a micro-array or assay.

32. (**NEW**) The apparatus of claim 31 further comprising:

a controller comprising a systems-biology platform that determines automatedly when the DNA sensor detects a genomic mutation indicating compromised ability to produce thiopurine S-methyltransferase enzyme.

33. (**NEW**) Sensor apparatus comprising:

a multi-functional array coupled programmably to a peptide or protein sensor, an antibody sensor, a carbohydrate sensor, or a cell sensor;

a positioning chip, coupled to one or more of the array sensors;

a therapeutic unit comprising a pill comprising a micro-pump, a polymer scaffold comprising hydrogel, or an implantable bio-MEMs chip comprising a medication reservoir; and

a controller that controls the therapeutic unit or the sensor array.

34. (**NEW**) Sensor apparatus comprising:

a multi-functional array coupled programmably to a peptide or protein sensor, an antibody sensor, a carbohydrate sensor, or a cell sensor;

wherein the peptide or protein sensor comprises an electrophoresis tag or micro-assay, or protein chip; the antibody sensor comprises a phagotope biochip; the carbohydrate sensor comprises a glycochip, or a whole blood glucose monitoring system; and the cell sensor comprises a bionic chip for cell-growth.

35. (**NEW**) The apparatus of claim 34 wherein:

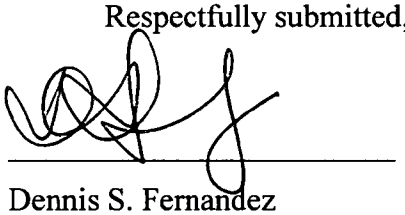
the sensor array couples further to a vector or virus vector sensor comprising a micro-array or assay with known sequenced virus attached, or a micro-array or assay that detects homologs; and to a DNA sensor comprising a micro-array or assay.

REMARKS

Applicant corrects the Information Disclosure Statements and the Specification as suggested by the Examiner, pursuant to the Office Action dated 05/18/2006.

New claims, 21-35, are added. Claims 1-10 are cancelled. Claims 11-20 are withdrawn.

Respectfully submitted,



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ELECTRONICALLY FILED ON May 29, 2007

PATENT
Attorney Docket No.: FERN-PO13

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 1019
Inventors: FERNANDEZ, D. S.	Group No.: 1631
Serial No.: 10/646,682	Examiner: MILLER, Marina
Filed: August 22, 2003	Customer No. 021971
For: **Integrated Biosensor and Simulation System for Diagnosis and Therapy**	

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT UNDER C.F.R. §1.111

Dear Sir:

Introductory Comments:

Applicants submit this Amendment in response to the Office communication dated November 29, 2006. This response/amendment is filed May 29, 2007 thus is timely filed. The Commissioner is authorized to charge any additional fees, which may be required, including petition fees and extension of time fees under 37 CFR 1.136(a) and/or applicable section, to Deposit Account No. 23-2415 (FERN-P013).

Reconsideration of the above-referenced application is respectfully requested in view of the following amendments and remarks.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 4 of this paper.

Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application. In the Office communication mailed November 29, 2006, the Examiner asserts that new claims 21-35 are directed to non-elected subject matter and are distinct from currently canceled claims 1-10 which were the object of Office Action mailed May 18, 2006. In order to be fully responsive, new claims 36-46 are presented, which are the same as or indistinct from canceled claims 1-10. Similarly to canceled claims 1-10, new claims 36-43 are directed to a biosensor and simulation system and method for using the same. Furthermore, independent claim 36 and 40 (canceled claims 1 and 6) incorporate embodiments encompassed by canceled claims 3 and 8.

Claims:

1. – 35. (Canceled)

36. **(New)** Integrated biosensor and simulation system comprising: a sensor for sensing a biological target to generate a signal; and a simulator for using the signal and a model of the target to generate a therapeutic or diagnostic output; and wherein said sensor is reconfigurable by said simulator.

37. **(New)** The system of claim 36 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

38. **(New)** The system of claim 36 wherein: the simulator generates the output according to a regulatory condition.

39. **(New)** The system of claim 36 wherein: the sensor couples to the simulator via a programmable switch.

40. **(New)** Automated sensor and simulation method comprising the steps of: sensing a biological target to generate a signal; simulating using the signal and a model of the target to generate a therapeutic or diagnostic output; and wherein said simulator reconfigures said sensor.

41. **(New)** The method of claim 40 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

42. **(New)** The method of claim 40 wherein: the simulator generates the output according to a regulatory condition.

43. **(New)** The method of claim 40 wherein: the sensor couples to the simulator via a programmable switch.

REMARKS

Claims 1-10 were rejected in an Office Action mailed May 18, 2006 ("Office Action"). Please reconsider the rejections in view of the foregoing amendments and remarks as set forth herein. Instant claims 36-43 correspond to claims 1-10, which were subject to examination and the rejections set forth in the Office Action.

I. Rejection under 35 USC §112, second paragraph

The rejection of claims 36-43 (canceled claims 1-10) is respectfully traversed for reasons set forth herein. The Examiner asserts that the inventions are not particularly pointed out or distinctly claimed for a plurality of response, each of which is addressed herein below.

1. **Claim 36 (canceled claims 1 and 7)**

Regarding claim 36, the claim particularly points out and distinctly claims a system comprising at least two components. In particular, claim 36 plainly recites an "Integrated biosensor and simulation system comprising: a sensor...and a simulator...". Therefore, the claim is clear and definite, because it would be understood that the claim is directed to an integrated system comprising a biosensor and simulation component. Furthermore, canceled claims 36-46 (claims 1-10) were previously understood to be system claims, where the Examiner asserted that claims 1-10 are directed to "a system and method" and claims 11-20 are directed to a network biosensor. (See, Restriction, mailed Feb. 28, 2006).

In any event, the claims must not be examined in a vacuum, but rather, must be interpreted in view of the full disclosure. Thus, in reading the specification (e.g., "Summary" section), one would comprehend that an "Integrated biosensor-simulation system combines one or more sensor to detect various conditions...and...simulator...". Therefore, the claim 1 is clear and definite as written.

Next, the Examiner asserts that it is unclear whether claim 36 is directed to a simulator that generates an output or whether a simulator uses a signal and a model wherein the model generates an output (i.e., therapeutic or diagnostic). Again, the plain meaning of the subject phrase is clear and definite, where claim 36 recites "a simulator for using the signal *and* a model of the target to generate a therapeutic or diagnostic output." (emphasis added) Clearly, the conjunction "and"

should indicate to the reader that the simulator utilizes the signal generated from the sensor, *and* a model for the biological target to generate an output (i.e., therapeutic or diagnostic). Furthermore, the specification provides ample characterization of a "simulator using system-biology model *and* sensor data adaptively to provide therapy, diagnosis, or other automated feedback [i.e., output]." (e.g., Summary section). Therefore, claim 1 is clear and definite as written.

2. Claim 36 (canceled claim 2)

Regarding claim 37, the Examiner asserts that it is unclear whether the claim is directed to an intended use of the sensor and/or the simulator and/or a result. Further, the Examiner asserts that it is unclear "what limitation of the sensor and simulator is intended". With respect to this latter assertion, it is not understood what is the source of the Examiner's misapprehension. The plain meaning of the limitation "the sensor is reconfigurable by the simulator" is unambiguous and distinct. The specification is replete with characterizations for sensor(s) that are reconfigurable (e.g., paragraphs[1] 0004, 0021-22, 0218, 0224, 0232). As the instant specification clearly sets forth, in one embodiment, a *reconfigurable* biocatalytic chip are software programmable from the simulator (e.g., systems-biology platform or through wireless external communication unit), which can result in activation, deactivation, manufactured or disassembled). (e.g., paragraph 0224). In another embodiment, "reconfigurable" means a sensor(s) can be personalized by the simulator, so that the sensor (e.g., tissue scaffold) is reconfigured based on the individual need. (e.g., paragraph 0225).

Therefore, whether reading the claim or the specification, it is quite unambiguous that the sensor(s) is reconfigurable by the simulator.

The Examiner's reference to an intended use or a result appears to be an extension of the misapprehension as to what is being claimed. Claim 36 merely recites that the sensor is reconfigurable by the simulator. Thus, it is not a result that is being reconfigured but the sensor. Further, the limitation is more than a mere intended use, because claim 36 is directed to a system where a sensor is capable of being reconfigured by a simulator and a simulator is capable of

[1] All references to the application/specification correspond to the published application, i.e., No. 2005/0043894A1)

reconfiguring the sensor. In other words, the subject limitation characterizes a material aspect of the system, with respect to the simulator and sensor. Therefore, claim 2 is clear and definite as written.

3. Claim 37 (canceled claim 3)

Regarding claim 37, the Examiner asserts that it is unclear what further limitation is intended with respect to the base claim 36. Claim 37 further limits the number/type of signal detected. For example, where base claim 36 is directed to a sensor for sensing a biological signal, dependent claim 38 further limits the base claim because the sensor is capable of sensing a second signal from a food material. The claim recites that the sensor generates a second signal which generates an output. The claim is directed to a system, so it is unclear why the Examiner refers to "method steps". (Office Action, page 9, lines 12-15).

Further, the plain meaning of claim 37 is unambiguous, where a signal corresponds to a biological target, as required by independent claim 36, and a *second* signal corresponds to a food material for consumption by the biological target. Therefore, one should comprehend claim 38 to further require a second signal, different from the first signal. In addition, the food material is not required to *have been* consumed. As written the claim, as further characterized in the specification, requires that the food material is sensed to produce a second signal, but there is no requirement that the sensor sense the food material after consumption (See, paragraphs 0106, 0154, 0157 and 0187-0189).

Regarding whether the simulator utilizes only the second signal or the first signal to produce an output, it is respectfully pointed out that since claim 38 (canceled claim 3) is a dependent claim, it incorporates the intervening claimed limitations. Therefore, as written, the claim requires both the first and second signal to produce an output.

Similarly, regarding whether the model of the base claim is also used in conjunction with the signals, claim 37is a dependent claim, thus one would readily comprehend that all the limitations of intervening claims are required (e.g., signal in base claim, model in base claim and second signal in instant dependent claim 38).

4. Claim 38 (canceled claim 4)

Regarding claim 38 the Examiner asserts that it is unclear what is "a regulatory condition" . The Examiner actually sets forth several different examples for interpretations of the term "regulatory condition", all of which fall within the scope of the limitation. Therefore, this is not a case of indefiniteness, but breadth or scope of the subject limitation. It is respectfully pointed out that the breadth of claims is not to be equated with indefiniteness. MPEP § 2173.04.

Furthermore, as to the issue raised with the limitation "the output", it is clear that the instant claim has antecedent support for the output as being "a therapeutic *or* diagnostic output". Therefore, it is not indefinite as to what is the output, since the plain meaning of output encompasses therapeutic or diagnostic.

5. Claim 39 (canceled claim 5)

The Examiner asserts that the limitation "couples" is vague, because it is not known whether this requires a physical connection or connection via a network. Further, the Examiner asserts that it is unclear whether "coupling" is a method step.

The claim requires that a sensor "couples to the simulator via a programmable switch". As recited in the base claim and further characterized in the specification, the components of the system can be physically coupled or coupled through communications such as wireless communications. (e.g., paragraphs 0005, 0019, 0021, 0049). Therefore, it appears there is a misapprehension of scope versus any issues of indefiniteness.

6. Claim 40 (canceled claims 6 and 7)

The Examiner asserts that it is unclear whether independent claim 41 is directed to a method or system. As the Examiner points out the claim is interpreted to mean it is directed to a method, thus it is unclear why this claim is rejected. The claim follows standard practice for reciting a method. Furthermore, all applicable dependent claims recite "The method...", obviating any purported ambiguity.

Regarding whether a signal and a model are utilized to generate an output, similar to the discussion above for the system claims, the method claim here is directed to simulating using the signal *and* model to generate an output. Again, the simulator generates the output using both the

signal and the model. The claim's plain meaning is distinct and clear. Furthermore, the specification is replete with description characterizing (e.g., paragraph 0098; describing a simulator compared sensed signals against a model or other software prediction to provide an output). In addition, the method requires generating an output. In sum, the plain meaning of the claim aloneor in conjunction with the specification is clear and distinct.

7. Claim 40 (canceled claim 7)

The Examiner asserts that is unclear whether "reconfiguring" is intended to be an additional step to "sensing" and "stimulating" recited in the base claim or is somehow to substitute one or more steps of the base claim. The claim is a dependent claim which further requires a simulator reconfigures a sensor. The plain meaning of the claim is clear and distinct, where an additional step of reconfiguration is required. Furthermore, the disclosure adequately characterizes the "reconfiguring" embodiment (e.g., paragraphs 0005, 0022, 0028, 0046, 0244).

8. Claim 41 (canceled claim 8)

The Examiner asserts the same grounds of rejection as those stated for claim 37. Claim 41(canceled claim 8) further limits the number/type of signal detected. For example, where the base claim is directed to a method requiring sensing, simulating and generating an output. Dependent claim 41 further limits the base claim because the sensor is capable of sensing a second signal from a food material.

Further, the plain meaning of claim 41 is unambiguous, where a signal corresponds to a biological target, as required by independent claim 40, and a *second* signal corresponds to a food material for consumption by the biological target. Therefore, one should comprehend claim 41to further require a second signal, different from the first signal. In addition, the food material is not required to *have been* consumed. As written the claim, as further characterized in the specification, requires that the food material is sensed to produce a second signal, but there is no requirement that the sensor sense the food material after consumption (See, paragraphs 0106, 0154, 0157 and 0187-0189).

9. Claim 43 (canceled claim 9)

The limitation "the output" is clear and distinct, because base claim clearly recites that output can be "therapeutic or diagnostic". Therefore, the instant claim encompasses therapeutic or diagnostic output.

In sum, the instant claims are clear and definite. Therefore, this rejection should be withdrawn.

II. Rejection under 35 USC § 112, first paragraph

Claims 1-10 (now claims 36-43) were canceled as failing to comply with the enablement requirement. This rejection is respectfully traversed. The Examiner sets forth *Wands* factors analysis, which is addressed in turn herein below. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1. Breadth of claims

The Examiner asserts that the claims are broad and that the specification does not provide specific guidance as to how to generate an unspecified signal, using an unspecified sensor, which senses an unspecified target, nor how to generate a diagnostic or therapeutic output.

There appears to be some misapprehension as to what are various key aspects of the invention. For example, as set forth in Figures 1-6, the invention is not limited to any particular sensor, target, simulator or output. Rather, one of the key aspects of the invention is the integration of various components in systems and methods to monitor individual, to simulate data and/or analyzing systems-biology software to generate diagnostic or therapeutic guidance.

Moreover, the specification provides numerous examples of the types of sensors that can be utilized with the methods or systems of the invention. For example, Figure 2 provides various sensors that can be utilized. Furthermore, Figure 1 illustrates a system envisaged by Applicant, which can be utilized in one or more methods of the invention. The system comprises a sensor unit, a systems biology platform which provides simulation (e.g., systems biology platform). Furthermore, the specification provides ample examples of sensors that are known in the art, such as MEMs, NEMS or microfluidic sensors (e.g., paragraphs 0050, 0052). Particular sensors disclosed include DNA sensors (e.g., paragraphs 0052, 0054, 0059), RNA sensors (e.g., paragraphs

0060, 0061), peptide/protein sensors (e.g., paragraphs 0062-0065), lipid/fatty acid sensor (e.g., paragraphs 0076), virus sensor (e.g., paragraph 0078) or carbohydrate sensor (e.g., paragraphs 0082). Therefore, specific examples of sensors and target molecules are adequately disclosed in the specification. Furthermore, the types of signals for various sensors are known in the art, as well as disclosed in the specification. (e.g., paragraph 0019). Moreover, the artisan will recognize that any sensor/target known in the art can be utilized in the methods/systems of the invention.

2. Nature of the invention

As discussed herein above, the claims are directed to a system and method comprising sensor and simulation components.

3. Prior art/predictability

The Examiner sets forth several examples of prior art systems for diagnosis of different conditions using various specific signals. (Office Action, pages 4-7). A patent need not teach, and preferably omits, what is well known in the art. Therefore, the Examiner appears to acknowledge that there are various sensors in the prior art that are utilized for provide signals, which can be utilized to generate an output, such as in diagnosis. Indeed, "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Notably, the Examiner does not set forth a single reasoned basis as to why there is unpredictability in integrating various sensors into systems or methods of the present invention. As such, the Examiner has not met the burden of providing evidence to support the assertion that there is unpredictability in practicing the claimed inventions, which can lead to undue experimentation.

4. The level of skill

The level of skill in the art is high. Therefore, the artisan can integrate what is known in the art with the novel disclosures of the instant specification to make and use the system and methods of the invention.

5. Working examples

The Examiner asserts that there are no working examples presented and that the specification does not teach how to make and use the invention, because no specific sensor, target or simulators are disclosed. Furthermore, the Examiner asserts that the specification does not teach how to diagnose a disease/condition or teach a system comprising an actual biosensor and simulator.

First, compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. See, MPEP § 2164.02. An example may be "working" or "prophetic." A working example is based on work actually performed. A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved. An applicant need not have actually reduced the invention to practice prior to filing. In *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987), as of Gould's filing date, no person had built a light amplifier or measured a population inversion in a gas discharge. The Court held that "The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." 822 F.2d at 1078, 3 USPQ2d at 1304 (quoting *In re Chilowsky*, 229 F.2d 457, 461, 108 USPQ 321, 325 (CCPA 1956)).

Second, the instant specification provides ample description of various sensors, targets and simulators (e.g., Section II(1), supra). Examples of sensors/targets include a metabolite sensor can measure serum homocysteine levels associated with increased risk of cervical cancer. (paragraph 0086). Further, a DNA sensor may detect common polymorphisms in one-carbon metabolic pathway, including mutations such as MTHFR, C677T, A1298C. (Id.). Additional examples, include a chemical sensor which senses levels of carcinogen, benzo(a)pyrene diol epoxide, a metabolic product found in tobacco smoke, known to cause 9p21 aberrations in peripheral blood lymphocytes in bladder cancer. (paragraph 0085). Yet another example, discloses a sensor can

monitor blood-flow to provide a signal that can be indicative of arterial pulse pressure, which signal can be plethysmography signal that can be produced by an implantable or non-implanted sensor (paragraph 0092). Furthermore, various methods known in the art are disclosed as a means for implanting sensors. (e.g., paragraphs 0094-0095). The foregoing are but a few examples provided in the instant specification, which provides a multitude of examples, each of which is adaptable to systems or methods of the present invention.

In addition, the specification provides various examples for a simulator component to be utilized with one or more sensors of the invention, i.e., a system comprising a sensor and simulator (e.g., paragraph 0028-0029, 0041-0048). Therefore, in view of the foregoing, it is factually inaccurate to assert that the specification does not disclose a system comprising a sensor and a simulator, or that the specification does not teach how to use systems/methods of the invention to generate an output, such as diagnosing a condition.

6. Amount of experimentation

The Examiner asserts that undue experimentation is necessary, because one of skill must randomly select a sensor, target, and must guess which signal and model to use for generating an unknown therapeutic or diagnostic output. There appears to be a misapprehension of what an artisan understands and would do in order to practice the claimed inventions.

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). As evidenced by the examples provided in the instant specification or by the art that Examiner notes (Office Action, pages 4-7), various sensors are known in the art.

The instant inventions are directed to systems/methods of integrated sensors and simulators, and where simulators can reconfigure sensors as needed. This is not the case of random selection or guesswork. Rather, the artisan would utilize one or more sensors known in the art in the systems and methods of the invention. For example, a clinician wanting to sense a target in someone susceptible to cancer (e.g., heavy smoker) would select diagnostic metrics known in the art (e.g., selection of cancer markers using DNA sensor disclosed in the instant specification and/or known

in the art). One novel aspect of the invention is integrating a sensor with a simulator (e.g., systems-biology platform) to interpret data to be analyzed and modeled to determine the diagnostic or therapeutic output.

In sum, the reasons set forth in the Office Action fail to establish a prima facie case for lack of enablement. Therefore, this rejection should be withdrawn.

III. Rejections under 35 USC §102

1. US 6,042,548 (Giuffre)

Claims 1-2, 4-7 and 9-10 were rejected (new claims 36-43) as being anticipated by US Patent 6,042,548 (Giuffre). This rejection is respectfully traversed.

The claims are directed to systems and methods requiring a sensor, a simulator and where the sensor is reconfigurable by the simulator. The Examiner asserts that Guiffre discloses a simulation using a signal and a model, where a sensor is reconfigured by a simulator (citing Fig. 3 and col. 6, lines 53-59). The reference does not disclose a sensor that is reconfigured by a simulator. In fact, as the Examiner points out, the reference discloses that data from a cardiovascular monitor is utilized to crate a simulated brain monitor means signal which it compares with an actual brain monitor means signal, and using a series of comparator means, constructs a hybrid signal with decreased artifact. (col. 6, ll. 55-59). In other words, the simulator does not actually reconfigure the sensor, but rather, constructs a hybrid signal from two sets of sensors. This does not meet the claimed requirement of "reconfiguring a sensor".

As recited in the instant claims, "reconfigurable" does not equate to utilizing different sensors to produce a hybrid signal, as asserted by the Examiner. For example, the instant specification discloses in one embodiment, a biocatalytic chip which is software programmable from the simulator (e.g., systems-biology platform or through wireless external communication unit), which can result in activation, deactivation, manufactured or disassembled). (e.g., paragraph 0224). In another embodiment, "reconfigurable" means a sensor(s) can be personalized by the simulator, so that the sensor (e.g., tissue scaffold) is reconfigured based on the individual need. (e.g., paragraph 0225). Thus, reconfigured in this sense encompasses reconfiguring a sensor or

multiple sensors, and not merging two sets of signals to reduce background/noise, as Giuffre discloses.

As such, the reference does not anticipate independent claims 36 and 40. Therefore, this rejection should be withdrawn.

2. US 6,542,858 (Grass)

Claims 1-2, 4-7 and 9-10 (new claims 36-43) were rejected as being anticipated by US Patent 6,542,858 (Grass). This rejection is respectfully traversed.

First, it is respectfully pointed out that the reference is not available under 35 USC 102(b), because it was published in April 1, 2003, while the instant application was filed in August 22, 2003. Presumably, the Examiner intended to assert this rejection under 35 USC 102(e).

The Examiner asserts that Grass discloses reconfiguring a sensor by a simulator (citing col. 12, line 52 through col. 13, line 32). Again, there appears to be some misapprehension as to what is claimed and what is disclosed with respect to the limitation "reconfigures". Upon examination of the entirety of the Grass disclosure, as well as a closer examination of the portions that the Examiner cites, Grass states that values for a given simulation model can be generated de novo or obtained from existing sources and that optimized adjustment parameter values of a given simulation model represent regression or stochastic analysis derived values. (Col. 12, ll. 53-65). The reference further discloses that input variables utilized for fitting include in vitro and in vivo data. (Id.). In sum, the disclosure is limited to the fitting of data points so as to allow correlation different data sets, and providing a fitted adjustment parameter to provide a constant in a model, so as to minimize deviation of correlation is minimized. (Col. 13, ll. 1-35).

Therefore, the reference does not disclose the claimed limitation of a simulator reconfiguring one or more sensors. As such, this rejection should be withdrawn.

IV. Rejection under 35 USC 103

Claims 3 and 8 (new claims 37 and 42) were rejected as being obvious over Grass and further in view of Quellette (Industrial Physics, pages 11-12, 1998). This rejection is respectfully traversed.

As discussed in Section III(2) above, Grass is deficient with respect to the claimed limitations of independent claims 36 and 40. Further, similar to Grass, Quellette does not teach or suggest the claimed limitation of a simulator reconfiguring one or more sensors. As such, Grass alone or in combination with Quellette does not render obvious claims 37 and 42. Therefore, this rejection should be withdrawn.

CONCLUSION

Applicants respectfully solicit the Examiner to expedite the prosecution of this patent application to issuance. Should the Examiner has any questions or believes it would beneficial as to any issues above, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Date: May 29 2007

By: 

Ray Akhavan
Registration No. 58,120

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ELECTRONICALLY FILED ON October 29, 2007

PATENT
Attorney Docket No.: FERN-PO13

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 1019
Inventors: Dennis Fernandez	Group No.: 1631
Serial No.: 10/646,682	Examiner: Eric S. Dejong
Filed: August 22, 2003	Customer No. 021971
For: Integrated Biosensor and Simulation System for Diagnosis and Therapy	

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT UNDER C.F.R. §1.111

Dear Sir:

Introductory Comments:

Applicants submit this Amendment in response to the Office Action mailed August 8, 2007. This response/amendment is filed October 26, 2007, thus is timely filed. The Commissioner is authorized to charge any additional fees, which may be required, including petition fees and extension of time fees under 37 CFR 1.136(a) and/or applicable section, to Deposit Account No. 23-2415 (FERN-PO13).

Reconsideration of the above-referenced application is respectfully requested in view of the following amendments and remarks.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 5 of this paper.

CLAIMS

What is claimed is:

1. – 35. (Canceled)

36. **(Currently Amended)** An ~~Integrated~~ integrated biosensor and simulation system comprising: ~~a~~at least one ~~sensor~~ biosensor for sensing a biological target to generate a signal; and a simulator for using the signal and a model of the target to generate a therapeutic or diagnostic output; and wherein said sensor is reconfigurable by said simulator.

37. **(Previously presented)** The system of claim 36 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

38. **(Previously presented)** The system of claim 36 wherein: the simulator generates the output according to a regulatory condition.

39. **(Previously presented)** The system of claim 36 wherein: the sensor couples to the simulator via a programmable switch.

40. **(Currently Amended)** ~~Automated sensor and simulation~~A method comprising the steps of: sensing with a biosensor a biological target to generate a signal; simulating with a simulator using the signal and a model of the target to generate a therapeutic or diagnostic output; and wherein said simulator reconfigures said ~~sensor~~biosensor.

41. **(Previously presented)** The method of claim 40 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

42. **(Previously presented)** The method of claim 40 wherein: the simulator generates the output according to a regulatory condition.

43. **(Previously presented)** The method of claim 40 wherein: the sensor couples to the simulator via a programmable switch.

44. (**New**) The method of claim 40, wherein said sensor is implanted in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

45. (**New**) The method of claim 40, wherein said biosensor comprises an array of at least two sensors.

46. (**New**) The method of claim 45, wherein said at least two sensors are capable of sensing two different biological targets.

47. (**New**) The method of claim 46, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

48. (**New**) The method of claim 40, wherein said reconfiguring comprises activating or deactivating said biosensor.

49. (**New**) The method of claim 45, wherein said reconfiguring comprises activating or deactivating at least one of said at least two sensors.

50. (**New**) The method of claim 40, wherein said reconfiguring comprise hardware reconfiguration.

51. (**New**) The system of claim 36, wherein said simulator is capable of activating or deactivating said sensor.

52. (**New**) The system of claim 36, wherein said sensor is capable of functioning in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

53. **(New)** The system of claim 36, wherein said biosensor comprises said at least one sensor and at least a second sensor.

54. **(New)** The system of claim 53, wherein said at least one sensor and said at least second sensor are capable of sensing two different biological targets.

55. **(New)** The system of claim 54, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

REMARKS

Applicant wishes to thank Examiner DeJong for extending the courtesy of a telephonic interview on September 17, 2007, with Applicant's representative Ray Akhavan. The Examiner's suggestions and comments were very helpful. In addition, Applicant thanks Examiner DeJong for withdrawal of certain rejections set forth in the Office Action mailed May 18, 2006.

Claims 36-55 are pending in this application. Claims 36-43 were previously pending, and new claims 44-55 are submitted herewith. The new claims do no present any new matter and are supported in the specification, such as in paragraphs 0018, 0023, 0040, 00047,0050-0090, 0233 (claims 44-48 and 52-55), Figure 2, paragraphs 0040, 0050, and 0233 (claim 49), paragraph 0022 (claim 50), paragraph 0232 (claim 51) which were subject to examination and the rejections set forth in the Office Action. It is earnestly believed that the claims are in a condition for allowance.

I. Rejection under 35 USC §112, second paragraph

Claims 40-43 were rejected as being vague and indefinite. It is believed that the grounds for the rejection are rendered moot in view of the instant amendments. Therefore, Applicant respectfully requests that this rejection be withdrawn.

II. Rejection under 35 USC § 101

Claims 40-43 were rejected as being directed to non-statutory subject matter. It is believed that the grounds for the rejection are rendered moot in view of the instant amendments. Therefore, Applicant respectfully requests that this rejection be withdrawn.

III. Rejections under 35 USC §102

Claims 36-43 were rejected as being anticipated by US Patent 6,042,548 (Giuffre). This rejection is respectfully traversed.

The claims are directed to systems and methods requiring a sensor, a simulator and where the sensor is reconfigurable by the simulator. It is asserted that Guiffre discloses a simulation using a signal and a model, where a sensor is reconfigured by a simulator (citing Fig. 3 and col. 4, lines 6-60 and col. 6, lines 53-59). However, in reviewing the reference, it is apparent that the reference discloses that data from a cardiovascular monitor is utilized to create a simulated brain monitor means signal which it compares with an actual brain monitor means signal, and using a series of comparator

means, constructs a hybrid signal with decreased artifact. (col. 6, ll. 55-59). In other words, the simulator does not actually reconfigure the sensor, but rather, constructs a hybrid signal from two sets of sensors. This does not meet the claimed requirement of "reconfiguring a sensor". As recited in the instant claims, "reconfigurable" does not equate to utilizing different sensors to produce a hybrid signal, as asserted by the Examiner. For example, the instant specification discloses in one embodiment, a biocatalytic chip which is software programmable from the simulator (e.g., systems-biology platform or through wireless external communication unit), which can result in activation, deactivation, manufactured or disassembled). (e.g., paragraph 0224). In another embodiment, "reconfigurable" means a sensor(s) can be personalized by the simulator, so that the sensor (e.g., tissue scaffold) is reconfigured based on the individual need. (e.g., paragraph 0225). Thus, reconfigured in this sense encompasses reconfiguring a sensor or multiple sensors, and not merging two sets of signals to reduce background/noise, as Giuffre discloses.

In addition, Giuffre does not teach or suggest the claimed embodiments comprised in the new claims. As such, Applicant respectfully requests that this rejection be withdrawn.

CONCLUSION

Applicant respectfully solicits the Examiner to expedite the prosecution of this patent applicant to issuance. Should the Examiner have any questions or believes it would be beneficial as to any issues above, the Examiner is encourage to telephone the undersigned.

Respectfully submitted,

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Date: Oct 29, 2007

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IN UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/646,682	Confirmation No. : 1019
Applicant	:	Dennis S. Fernandez	
Filed	:	August 22, 2003	
Art Unit	:	1631	
Examiner	:	Eric S. Dejong	
Docket No.	:	FERN-P013	
CUSTOMER NO.	:	021971	
Title	:	Integrated Biosensor and Simulation Systems for Diagnosis and Therapy	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT

This responds to 12/02/08 Office Action.

Listing of Claims:

1-35. **(Canceled)**

36. **(CURRENTLY AMENDED)** A[[n]] systems-biology platform-based integrated biosensor and simulation system comprising:

at least one implantable biosensor for sensing a biological target to generate a signal; and

a simulator comprising a systems-biology platform for using the signal and a model of the target to generate a therapeutic or diagnostic output;

wherein said sensor is reconfigurable by said simulator, whereby the simulator automatically integrates the target biosensing with in-vivo modeling to simulate the biological target as a whole organism using the systems-biology platform, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, [[a therapeutic reservoir,]] or a DNA microarray.

37. **(Previously presented)** The system of claim 36 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

38. **(Previously presented)** The system of claim 36 wherein: the simulator generates the output according to a regulatory condition.

39. **(Previously presented)** The system of claim 36 wherein: the sensor couples to the simulator via a programmable switch.

40. **(CURRENTLY AMENDED)** A systems-biology platform-based method comprising the steps of:

sensing with an implantable biosensor a biological target to generate a signal; and

simulating with a simulator comprising a systems-biology platform using the signal and a model of the target to generate a therapeutic or diagnostic output; wherein said simulator reconfigures said biosensor, whereby the simulator automatically integrates the target biosensing with in-vivo modeling to simulate the biological target as a whole organism using the systems-biology platform, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, [[a therapeutic reservoir,]] or a DNA microarray.

41. **(Previously presented)** The method of claim 40 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

42. **(Previously presented)** The method of claim 40 wherein: the simulator generates the output according to a regulatory condition.

43. **(Previously presented)** The method of claim 40 wherein: the sensor couples to the simulator via a programmable switch.

44. **(Previously presented)** The method of claim 40, wherein said sensor is implanted in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

45. **(Previously presented)** The method of claim 40, wherein said biosensor comprises an array of at least two sensors.

46. **(Previously presented)** The method of claim 45, wherein said at least two sensors are capable of sensing two different biological targets.

47. **(Previously presented)** The method of claim 46, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

48. **(Previously presented)** The method of claim 40, wherein said reconfiguring comprises activating or deactivating said biosensor.

49. **(Previously presented)** The method of claim 45, wherein said reconfiguring comprises activating or deactivating at least one of said at least two sensors.

50. **(Withdrawn)**

51. **(Previously presented)** The system of claim 36, wherein said simulator is capable of activating or deactivating said sensor.

52. **(Previously presented)** The system of claim 36, wherein said sensor is capable of functioning in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

53. **(Previously presented)** The system of claim 36, wherein said biosensor comprises said at least one sensor and at least a second sensor.

54. **(Previously presented)** The system of claim 53, wherein said at least one sensor and said at least second sensor are capable of sensing two different biological targets.

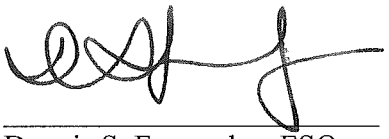
55. **(Previously presented)** The systems of claim 54, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody,

antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

REMARKS

Applicant amends independent claims 36 and 40 patentably to distinguish cited art, particularly distinguishing Porat by removing the "therapeutic reservoir" limitation, and also distinguishing Giuffre by specifying more particularly that the simulator of the claimed invention is directed to "systems-biology platform" that automatically integrates target biosensing with in-vivo modeling to simulate the biological target as a whole organism.

Respectfully submitted,



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IN UNITED STATES PATENT AND TRADEMARK OFFICE

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Applicant	:	Dennis S. Fernandez	
Filed	:	August 22, 2003	
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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT

This responds to Notice of Non-Compliant Amendment mailed 1/29/2009.

Listing of Claims:

1-35. **(Canceled)**

36. **(CURRENTLY AMENDED)** A[[n]] systems-biology platform-based integrated biosensor and simulation system comprising:

at least one implantable biosensor for sensing a biological target to generate a signal; and

a simulator comprising a systems-biology platform for using the signal and a model of the target to generate a therapeutic or diagnostic output;

wherein said sensor is reconfigurable by said simulator, whereby the simulator automatically integrates the target biosensing with in-vivo modeling to simulate the biological target as a whole organism using the systems-biology platform, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, [[a therapeutic reservoir,]] or a DNA microarray.

37. **(Previously presented)** The system of claim 36 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

38. **(Previously presented)** The system of claim 36 wherein: the simulator generates the output according to a regulatory condition.

39. **(Previously presented)** The system of claim 36 wherein: the sensor couples to the simulator via a programmable switch.

40. **(CURRENTLY AMENDED)** A systems-biology platform-based method comprising the steps of:

sensing with an implantable biosensor a biological target to generate a signal; and

simulating with a simulator comprising a systems-biology platform using the signal and a model of the target to generate a therapeutic or diagnostic output; wherein said simulator reconfigures said biosensor, whereby the simulator automatically integrates the target biosensing with in-vivo modeling to simulate the biological target as a whole organism using the systems-biology platform, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, [[a therapeutic reservoir,]] or a DNA microarray.

41. **(Previously presented)** The method of claim 40 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

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44. **(Previously presented)** The method of claim 40, wherein said sensor is implanted in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

45. **(Previously presented)** The method of claim 40, wherein said biosensor comprises an array of at least two sensors.

46. **(Previously presented)** The method of claim 45, wherein said at least two sensors are capable of sensing two different biological targets.

47. **(Previously presented)** The method of claim 46, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

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49. **(Previously presented)** The method of claim 45, wherein said reconfiguring comprises activating or deactivating at least one of said at least two sensors.

50. **(Withdrawn)** The method of claim 40, wherein said reconfiguring comprise hardware reconfiguration.

51. **(Previously presented)** The system of claim 36, wherein said simulator is capable of activating or deactivating said sensor.

52. **(Previously presented)** The system of claim 36, wherein said sensor is capable of functioning in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

53. **(Previously presented)** The system of claim 36, wherein said biosensor comprises said at least one sensor and at least a second sensor.

54. **(Previously presented)** The system of claim 53, wherein said at least one sensor and said at least second sensor are capable of sensing two different biological targets.

55. **(Previously presented)** The systems of claim 54, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

REMARKS

Applicant amends independent claims 36 and 40 patentably to distinguish cited art, particularly distinguishing Porat by removing the "therapeutic reservoir" limitation, and also distinguishing Giuffre by specifying more particularly that the simulator of the claimed invention is directed to "systems-biology platform" that automatically integrates target biosensing with in-vivo modeling to simulate the biological target as a whole organism.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	**Dennis S. Fernandez**	Attorney Docket No.:	**FERN-P013**
Serial No.:	**10/646,682**	Group Art Unit:	**1631**
Filed:	**08/22/2003**	Examiner:	**DeJong, Eric S**
Title:	**Integrated biosensor and simulation system for diagnosis and therapy**		

Confirmation No. **1019**

AMENDMENT

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

This responds to Office Action dated 9/2/2009.

Listing of Claims:

1-35. **(Canceled)**

36. **(CURRENTLY AMENDED)** A systems-biology platform-based integrated biosensor and simulation system comprising:

at least one implantable biosensor for sensing a biological target to generate a signal; and

a simulator comprising a systems-biology platform for using the signal and a model of the target to generate a therapeutic or diagnostic output;

wherein said sensor is reconfigurable by said simulator, whereby the simulator automatically integrates the target biosensing with in-vivo modeling to simulate the biological target as a whole organism using the systems-biology platform that comprises computational modeling hardware and software analysis genomics, proteomics, computational chemistry, pharmacogenomics, computational biology, computational biophysics, computational cell behavior, pharmacokinetics, metabolomics, and transcriptomics automated tools, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, a therapeutic reservoir, a probe arranger, or a DNA microarray.

37. **(Previously presented)** The system of claim 36 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

38. **(Previously presented)** The system of claim 36 wherein: the simulator generates the output according to a regulatory condition.

39. **(Previously presented)** The system of claim 36 wherein: the sensor couples to the simulator via a programmable switch.

40. **(CURRENTLY AMENDED)** A systems-biology platform-based method comprising the steps of:

sensing with an implantable biosensor a biological target to generate a signal; and

simulating with a simulator comprising a systems-biology platform using the signal and a model of the target to generate a therapeutic or diagnostic output; wherein said simulator reconfigures said biosensor, whereby the simulator automatically integrates the target biosensing with in-vivo modeling to simulate the biological target as a whole organism using the systems-biology platform that comprises computational modeling hardware and software analysis genomics, proteomics, computational chemistry, pharmacogenomics, computational biology, computational biophysics, computational cell behavior, pharmacokinetics, metabolomics, and transcriptomics automated tools, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, a therapeutic reservoir, a probe arranger, or a DNA microarray.

41. **(Previously presented)** The method of claim 40 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

42. **(Previously presented)** The method of claim 40 wherein: the simulator generates the output according to a regulatory condition.

43. **(Previously presented)** The method of claim 40 wherein: the sensor couples to the simulator via a programmable switch.

44. **(Previously presented)** The method of claim 40, wherein said sensor is implanted in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

45. **(Previously presented)** The method of claim 40, wherein said biosensor comprises an array of at least two sensors.

46. **(Previously presented)** The method of claim 45, wherein said at least two sensors are capable of sensing two different biological targets.

47. **(Previously presented)** The method of claim 46, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

48. **(Previously presented)** The method of claim 40, wherein said reconfiguring comprises activating or deactivating said biosensor.

49. **(Previously presented)** The method of claim 45, wherein said reconfiguring comprises activating or deactivating at least one of said at least two sensors.

50. **(Withdrawn)** The method of claim 40, wherein said reconfiguring comprise hardware reconfiguration.

51. **(Previously presented)** The system of claim 36, wherein said simulator is capable of activating or deactivating said sensor.

52. **(Previously presented)** The system of claim 36, wherein said sensor is capable of functioning in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

53. **(Previously presented)** The system of claim 36, wherein said biosensor comprises said at least one sensor and at least a second sensor.

54. **(Previously presented)** The system of claim 53, wherein said at least one sensor and said at least second sensor are capable of sensing two different biological targets.

55. **(Previously presented)** The systems of claim 54, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

REMARKS

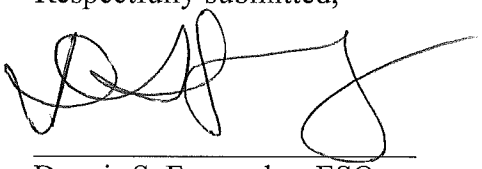
Re Information Disclosure Statement Examiner annotation that "copies of cited art not provided", applicant respectfully submits that copies of such cited foreign patent documents were in-fact provided previously, as evidenced properly in PAIR (see attached listing of PAIR image file wrapper with said foreign references indicated).

To overcome 35.USC.112 1st and 2nd-paragraph rejection of claims 36-49 and 51-55, applicant amends independent claims 36 and 40 to particularly point out and distinctly claim the subject matter which applicant regards as the invention, as well as comply with written description requirement, particularly specifying structural and functional limitation (i.e., not merely abstract scientific disciplines) such that systems-biology platform (Fig.3a) comprises "computational modeling hardware and software analysis" genomics, proteomics (para.124), computational chemistry (para.125), pharmacogenomics (para.126), computational biology, computational biophysics, computational cell behavior (para.127), pharmacokinetics (para.128), metabolomics (para.129), and transcriptomics (para.130) automated tools, whereby such computational modeling hardware and software analysis automated tools are described in specification pages 36-38 in such a way to reasonably convey to one of skilled in the relevant art that inventor at the time the application was filed had possession of the claimed invention.

Further to overcome 35.USC.103a rejection of claims 36-49 and 51-55 over Porat and Giuffre, applicant respectfully submits that such cited prior art neither teach, suggest nor motivate in any predictable or common sense "systems-biology platform" comprising

computational modeling hardware and software analysis genomics, proteomics, computational chemistry, pharmacogenomics, computational biology, computational biophysics, computational cell behavior, pharmacokinetics, metabolomics, and transcriptomics automated tools, as required by applicant's invention now claimed herein.

Respectfully submitted,



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IN UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/646,682	Confirmation No. : 1019
Applicant(s)	:	Dennis S. Fernandez	
Filed	:	August 22,2003	
Art Unit	:	1631	
Examiner	:	Eric S. Dejong	
Docket No.	:	FERN-P013	
CUSTOMER NO.	:	021971	
Title	:	Integrated Biosensor and Simulation Systems for Diagnosis and Therapy	

Commissioner for Patents
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Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

This RCE application responds to 08/07/08 Advisory Action and 5/14/2008 Final Action.

Listing of Claims:

1-35. **(Canceled)**

36. **(CURRENTLY AMENDED)** An integrated biosensor and simulation system comprising:

at least one implantable biosensor for sensing a biological target to generate a signal; and

a simulator for using the signal and a model of the target to generate a therapeutic or diagnostic output; [[and]]

wherein said sensor is reconfigurable by said simulator, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, a therapeutic reservoir, or a DNA microarray.

37. **(Previously presented)** The system of claim 36 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

38. **(Previously presented)** The system of claim 36 wherein: the simulator generates the output according to a regulatory condition.

39. **(Previously presented)** The system of claim 36 wherein: the sensor couples to the simulator via a programmable switch.

40. **(CURRENTLY AMENDED)** A method comprising the steps of:

sensing with an implantable biosensor a biological target to generate a signal; and

simulating with a simulator using the signal and a model of the target to generate a therapeutic or diagnostic output; [[and]] wherein said simulator

reconfigures said biosensor, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, a therapeutic reservoir, or a DNA microarray.

41. **(Previously presented)** The method of claim 40 wherein: the sensor senses a food material for consumption by the biological target to generate a second signal, the simulator further using the second signal to generate the therapeutic or diagnostic output.

42. **(Previously presented)** The method of claim 40 wherein: the simulator generates the output according to a regulatory condition.

43. **(Previously presented)** The method of claim 40 wherein: the sensor couples to the simulator via a programmable switch.

44. **(Previously presented)** The method of claim 40, wherein said sensor is implanted in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

45. **(Previously presented)** The method of claim 40, wherein said biosensor comprises an array of at least two sensors.

46. **(Previously presented)** The method of claim 45, wherein said at least two sensors are capable of sensing two different biological targets.

47. **(Previously presented)** The method of claim 46, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

48. **(Previously presented)** The method of claim 40, wherein said reconfiguring comprises activating or deactivating said biosensor.

49. **(Previously presented)** The method of claim 45, wherein said reconfiguring comprises activating or deactivating at least one of said at least two sensors.

50. **(Withdrawn)**

51. **(Previously presented)** The system of claim 36, wherein said simulator is capable of activating or deactivating said sensor.

52. **(Previously presented)** The system of claim 36, wherein said sensor is capable of functioning in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

53. **(Previously presented)** The system of claim 36, wherein said biosensor comprises said at least one sensor and at least a second sensor.

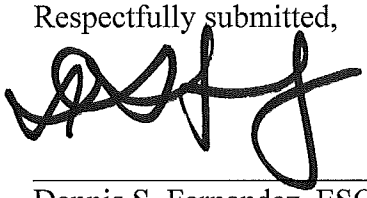
54. **(Previously presented)** The system of claim 53, wherein said at least one sensor and said at least second sensor are capable of sensing two different biological targets.

55. **(Previously presented)** The systems of claim 54, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

REMARKS

Applicant amends independent claims patentably to distinguish cited art.

Respectfully submitted,



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor: Dennis S. Fernandez | Attorney Docket No.: FERN-P013

Serial No.: 10/646,682 | Group Art Unit: 1631

Filed: 08/22/2003 | Examiner: Eric S. Dejong

Confirmation No.: 1019

Title: Integrated Biosensor and Simulation System for Diagnosis and Therapy

PRELIMINARY AMENDMENT

Mail Stop Amendment
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P.O. Box 1450
Alexandria, VA 22313-1450

This responds via RCE-application to FINAL Office Action dated 05/27/09.

Listing of Claims:

1-35. **(Canceled)**

36. **(CURRENTLY AMENDED)** A systems-biology platform-based integrated biosensor and simulation system comprising:

at least one implantable biosensor for sensing a biological target to generate a signal; and

a simulator comprising a systems-biology platform for using the signal and a model of the target to generate a therapeutic or diagnostic output;

wherein said sensor is reconfigurable by said simulator, whereby the simulator automatically integrates the target biosensing with in-vivo modeling to simulate the biological target as a whole organism using the systems-biology platform that comprises genomics, proteomics, computational chemistry, pharmacogenomics, computational biology, computational biophysics, computational cell behavior, pharmacokinetics, metabolomics, and transcriptomics, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, a therapeutic reservoir, a probe arranger, or a DNA microarray.

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40. **(CURRENTLY AMENDED)** A systems-biology platform-based method comprising the steps of:

sensing with an implantable biosensor a biological target to generate a signal; and

simulating with a simulator comprising a systems-biology platform using the signal and a model of the target to generate a therapeutic or diagnostic output; wherein said simulator reconfigures said biosensor, whereby the simulator automatically integrates the target biosensing with in-vivo modeling to simulate the biological target as a whole organism using the systems-biology platform that comprises genomics, proteomics, computational chemistry, pharmacogenomics, computational biology, computational biophysics, computational cell behavior, pharmacokinetics, metabolomics, and transcriptomics, such reconfiguration thereby reconfiguring a biocatalytic chip, a logic device, a tissue scaffold, a therapeutic reservoir, a probe arranger, or a DNA microarray.

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43. **(Previously presented)** The method of claim 40 wherein: the sensor couples to the simulator via a programmable switch.

44. **(Previously presented)** The method of claim 40, wherein said sensor is implanted in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

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47. **(Previously presented)** The method of claim 46, wherein said different biological targets are selected from a group consisting of DNA, RNA, peptide, antibody, antigen, tissue factor, virus, lipid, fatty acid, steroid, neurotransmitter, carbohydrate, free radical, neural, chemical, metabolite and cell.

48. **(Previously presented)** The method of claim 40, wherein said reconfiguring comprises activating or deactivating said biosensor.

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50. **(Withdrawn)** The method of claim 40, wherein said reconfiguring comprise hardware reconfiguration.

51. **(Previously presented)** The system of claim 36, wherein said simulator is capable of activating or deactivating said sensor.

52. **(Previously presented)** The system of claim 36, wherein said sensor is capable of functioning in a subject's mouth, larynx, blood vessel, vein, nose, ear, eye, heart, brain, lymph node, lung, breast, stomach, pancreas, kidney, colon, rectum, ovary, uterus, bladder or prostate.

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REMARKS

Re 35.USC.103a Examiner rejection of claims 36-49 and 51-55 over Porat and Giuffre, Applicant amends claims to specify that the systems-biology platform comprises "genomics, proteomics, computational chemistry, pharmacogenomics, computational biology, computational biophysics, computational cell behavior, pharmacokinetics, metabolomics, and transcriptomics."

Respectfully submitted,

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